Overexpression of Amphiregulin in the Epidermis of Transgenic Mice Induces a Psoriasis-Like Cutaneous Phenotype

To the Editor:

It has come to our attention that the review article entitled "Animal models of psoriasis – what can we learn from them" by Dr Michael P. Schön (Schön, 1999), which was published recently in the *Journal of Investigative Dermatology*, has omitted mentioning what we believe to be an important transgenic psoriasis-like mouse model. This model, in which we have overexpressed the heparin-binding EGF-related ligand Amphiregulin (AR) in the epidermis, produces a cutaneous phenotype that strongly resembles psoriasis and was first reported by our research group in November 1997 (Cook *et al*, 1997). In this mouse model, transgenic mice with a K14 enhancer/promoter-driven AR gene targeted to the epidermis displayed a macroscopic phenotype that included extensive areas of scaling and erythematous skin with marked alopecia. Moreover, histologic examination of these AR-expressing mice also revealed hyperkeratosis, focal parakeratosis, acanthosis, mixed leukocytic infiltration that included both CD3-positive T cells and neutrophils in the dermis and epidermis, and a tortuous dermal vasculature. We have concluded that our results reveal AR to exert activities in the skin that are distinct (e.g., leukocytic infiltration) from another transgenic EGF-ligand (transforming growth factor-α), or other cytokines. Furthermore, aberrant overexpression of AR might be involved in the pathophysiology of psoriasis as we and colleagues have shown that it is consistently overexpressed in involved psoriatic epidermis, when compared with normal or uninvolved epidermis (Cook *et al*, 1992; Hardas *et al*, 1992; Elder *et al*, 1993; Stoll *et al*, 1994; Piepkorn, 1996).

Recent observations have also implicated the non-HLA keratinocyte structural "S" or corneodesmosin gene as a potential psoriasis susceptibility gene located in close proximity to the MHC region of human chromosome 6 (Allen *et al*, 1999; Zhou and Chaplin, 1993; Tazi Ahnini *et al*, 1999). It has been speculated that defects in the function of the corneodesmosin differentiation antigen could lead to barrier disruption and initiate increased susceptibility to psoriatic lesion formation (Allen *et al*, 1999). Because recent reports have implicated AR as a wounding- or barrier disruption-associated factor (Liou *et al*, 1997; Stoll *et al*, 1997), we have therefore speculated that wound-induced AR expression may be involved in the pathogenesis of lesion formation, and in triggering lesion formation in patients with psoriasis that display the Koebner (isomorphic) response (Cook *et al*, 1997; Piepkorn *et al*, 1998). Thus cutaneous events initiating or mimicking abnormal wound re-epithelialization or barrier disruption responses (e.g., perturbed AR expression, defective S-gene expression) may emerge as a common pathway to psoriatic lesion formation.

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